Nanotechnology Discovery Saves Lives

Largest biological simulation provides genetic answers to aid medicine

Quick read
New medicines that save lives by combating drug-resistant bacteria —such as Staph (Staphylococcus aureus) —are just one of the results of the largest biological simulation ever.

Nanoscience—the study of things of "little" importance, one might quip—led to the largest biological simulation ever, which helped Los Alamos scientists decode genetic information. The methodology paved the way for developing new antibiotics and modeling the entire protein synthesis process—a process crucial to saving lives.

The body comprises enumerable nanofactories called ribosomes that work overtime to keep us alive. In each of our trillions of cells, a million ribosomes create proteins—chains of amino acids—that are the basis of life. A quintillion protein factories rebuild our entire body every seven years.

Ribosome study is nothing new but, "only now we can use supercomputers to investigate, in atomic detail, how this very complex machine really works," says Los Alamos National Laboratory theoretical biologist Kevin Sanbonmatsu. "It has been the holy grail and now our team at Los Alamos is making it happen."

Sanbonmatsu and Theoretical Biology and Biophysics Group Leader Chang-Shung Tung created the first atomic-level computer model of a single ribosome.

Sanbonmatsu and his team hope their 3D simulations can solve conflicting interpretations about ribosomes. Secondly, this technology will provide information required to design new medicine to combat drug-resistant bacteria, such as the prevalent Staph (Staphylococcus aureus), which causes many diseases and fatal infections such as food poisoning.

The Molecular-Dynamics Code

A ribosome's base parts were a mystery not too long ago, until 2000 when researchers solved the 3D atomic-level structure of each of the ribosome's two subunits. This research inspired Sanbonmatsu and Tung, who fit these asymmetrical subunits into a single mathematical representation and built a computer code to represent how the constituent atoms and molecules interact. They soon used their simulation work to find the tRNA's route into the rat's nest of the ribosome.

Their first model was the largest biomolecular-dynamics simulation ever done, encompassing more than 2.5 million atoms. Sanbonmatsu was warned this project was too ambitious for a newcomer, but he disproved critics and won a federal Presidential Early Career Award for Scientists and Engineers.

Sanbonmatsu's team's simulation computed the forces among atoms to determine the path of least resistance—the minimum-energy path. Viewing the results was extraordinarily time-consuming. After months of staring at each frame, viewing every atom, he found the invisible entry channel. Only 68 of the ribosome's 5,000 amino acids interacted with tRNA during entry at a ribosomal gate; the simulation revealed the end of the tRNA with the attached amino acid was deflected to avoid the barrier and get inside the ribosome's interior. In short, the model exposed how a ribosome rejects the wrong tRNA. For the first time, researchers learned that tRNA delivered important genetic information. Additionally, this data suggests tRNA might have existed long before the ribosome, facilitating protein synthesis in pre-life systems.

Important Nanotechnology Developments
While the origin of its name is miniscule—a billionth of a part, the core of atoms—nanotechnology is an extraordinary part of everyday life. There are some 600 commercial products available (e.g., cosmetics, sunscreen, clothing, home furnishings, sports, and electronic equipment) where nanotechnology plays a manufacturing role. Nanoscience enables improvements in medical diagnostics and drug delivery, bioscience, chemical sensing, military platforms, and nuclear defense systems and even helped Los Alamos National Laboratory (LANL) create a supreme superconductor. Sanbonmatsu's team is also preparing a new ribosomal simulation code for Roadrunner, LANL's world's most powerful computer.

Pushing Frontiers

In the second half of 2008, Los Alamos National Laboratory made significant advances in its primary mission: safeguarding the U.S. nuclear deterrent and pushing the frontiers of science on multiple fronts.
The national stockpile stewardship program achieved a major milestone in September with the production of the first life-extended W76-1 ballistic missile warhead for Trident submarines. The achievement culminated more than a decade of work by scientists and engineers at Los Alamos and across the nuclear weapons complex-including two crucial experiments conducted by the Laboratory's Hydrodynamic Experiments Division.
Another highlight: Roadrunner reached a new performance record of 1.105 petaflops, keeping it atop the list of the world's fastest supercomputers. Built by IBM for the Lab, Roadrunner was the first computer the crack the petaflop barrier: one thousand TRILLION operations per second. Initial applications will range widely: studying in great detail the evolution of HIV... exploring deeply the formation—as well as deformation—of metallic nanowires...and-toward producing biofuels more efficiently-unraveling the processes by which bacteria break down cellulose.
Safety and environmental stewardship were again a major theme for our work in the latter half of 2008. In November, the last group of unvented high-activity drums left Los Alamos for the Waste Isolation Pilot Plant near Carlsbad. That shipment fulfilled a commitment to the Defense Nuclear Facilities Safety Board to prioritize disposal of the highest-activity transuranic wastes stored at the Lab.
Los Alamos also strengthened security, ensuring that nearly six dozen classified and unclassified computing systems are managed and operated securely. The Lab has now complied with all 14 security actions mandated two years ago by the Department of Energy. And, through our program to recruit cognizant systems engineers, we met the crucial need for sufficient numbers of engineers to keep vital mechanical and electrical safety systems functioning properly in our nuclear facilities.
The latter half of 2008 proved once again why Los Alamos is the nation's premier institution for scientific research. Capping the list of accomplishments was a new technology called MagViz that could eventually provide increased security at major airports. Based on medical MRI technology, MagViz can identify contents of bottles and other containers, distinguishing potentially hazardous liquids from the harmless shampoos and perfumes a traveler might carry onboard a jet. MagViz was demonstrated successfully in December at Albuquerque's airport.
We continued a long tradition of supporting U.S. space exploration. A NASA mission, launched in October to probe the far edge of the solar system from a high Earth orbit, carried a Los Alamos device called the High Energy Neutral Atom Imager. Its goal: to detect atoms emitted from a region where the outermost reaches of our solar system meet the vast interstellar space-giving us a panoramic view of this gateway to the galaxy.
Closer to home, Los Alamos continues to explore solutions to the energy needs of tomorrow. For example, scientists at the Lab hope to use tiny semiconductors called quantum dots to convert sunlight to electricity more efficiently than is possible with current solar panels-and to create new, efficient solid-state lighting.
Equally electrifying, Los Alamos materials scientists are helping unravel the mysteries of superconductivity. During the latter half of the year, LANL researchers identified entirely new mechanisms for superconductivity that could form the basis for new superconducting materials.
Underscoring the wealth of scientific talent at the Lab, Bob Albers, Paul Johnson, and Kurt Sickafus were named Laboratory Fellows in December. These three Fellows represent diverse disciplines, including theoretical physics, energy science, and geophysics.

Los Alamos may be one of the world's great technology incubators, yet we also strive to help others develop new ideas and products. In January, the Lab selected four young local companies as the newest recipients of awards from the LANS Venture Acceleration Fund. LANS, which manages and operates the Lab, supports the fund through donations from its earnings.

The Lab and LANS also teamed last September with a venture capital firm and a local venture capital fund to spin off technology developed by Lab scientists, with an emphasis on creating companies in Northern New Mexico. The Lab could contribute up to one million dollars to the initiative over the first three years.

We also are pushing to build top-flight research facilities for the future. In July 2008, workers hoisted the final steel beam atop the skeleton of what will be the Radiological Laboratory Utility Office Building, part of the Lab's Chemistry and Metallurgy Research Replacement Project. Once completed, the CMRR nuclear facility will house several of the Lab's mission-critical projects, including analytical chemistry, materials characterization, and actinide research and development capabilities. They'll be relocated from their current location in the historic—yet antiquated—Chemical and Metallurgy Research building at Technical Area 3.

In December, Los Alamos welcomed hundreds of employees who transferred from KSL, the subcontractor whose work the Lab brought in-house. The move was geared to improve efficiency and reduce costs associated with site-support services, including maintenance, waste removal, and custodial work.

Throughout the Lab's history, Los Alamos has helped play a vital role in the surrounding communities, and in 2008, that tradition continued. Lab employees pledged a million dollars, and LANS matched one hundred percent: a record Los Alamos contribution to United Way of TWO MILLION dollars. Contributions from the Lab and LANS also helped fund dozens of nonprofit organizations and scholarship programs, including a LANS donation of $500,000 to a LANL Foundation scholarship named for former long-time New Mexico Senator Pete Domenici.

These accomplishments and many more added up to a strong year. Our customer, the National Nuclear Security Administration, reached the same conclusion in its very favorable assessment of the Lab's performance for fiscal year 2008. It's unmistakable: the extraordinary talent, commitment, and creativity that Los Alamos employees dedicate every day to national security science and the betterment of their communities.